Omega-3 Fatty Acid Supplementation Stimulates α-Tocopherol Incorporation in Erythrocyte Membranes in Adult Men

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Diets recommended to prevent cancer, heart disease, and diabetes involve reducing total fat and cholesterol and replacing saturated fat with polyunsaturated fats (PUFA) of both the n-3 and n-6 types. Implementing these recommendations often results in the incorporation of unsaturated fatty acyl groups in membrane phospholipids.[1–6] It is believed[7,8] that consuming PUFA diets depletes body vitamin E stores due to antioxidant activity.[9] Some experts therefore recommend vitamin E supplements with high PUFA diets.[9,10] Fish oils are highly unsaturated and are readily peroxidized.[11,12] We studied the effects of fish oil and vitamin E supplements on red cell membrane composition and other properties when total fat intake was similar to the typical USA diet.

Men, nonsmokers, ages 24–57, were recruited and screened to exclude any with health problems or unusual dietary habits. A basal diet of commonly available foods was fed for 28 weeks with 15 g/day of either placebo oil (PO) or fish oil concentrate (FOC) (ROPUFA-50%®, supplied by Hoffmann-La Roche Inc. Nutley, NJ). The diet and oil supplement together provided 40% of calories from fat. Supplements were 15 g placebo oil (PO) in 1 g soft gelatin capsules fortified with

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TABLE 1. Estimated Daily Intakes by Subjects

Nutrient	Placebo period	Fish oil periods
Fat (percent of energy)	39	39
Carbohydrate (percent of energy)	45	45
Protein (percent of energy)	16	16
Cholesterol (mg/d at 2800 kcal)	360	360
Fatty acid intake (g/d at 2800 kcal)		
Saturates (total)	33	29
palmitate	20	18
stearate	9	7
Monounsaturates (total)	46	42
oleate	44	39
Polyunsaturates (total)	27	33
18:3 (n-3)	2	2
20:5 (n-3)	0	5
22:6 (n-3)	0	2
18:2 (n-6)	25	23

1 IU of *dl*-α-tocopherol/capsule for 10 weeks; 15 g of fish oil concentrate (FOC) in similar capsules containing 1 g FOC and 1 IU *dl*-α-tocopherol for the second 10 weeks; and the FOC capsules plus a daily 200 IU *dl*-α-tocopherol capsule for the final 8 weeks. Daily nutrient and fatty acid intakes are given in TABLE 1. At the end of each experimental period, erythrocytes were collected and lysed,[13] and vitamin E analyses[14] were performed with intact cells and membrane preparations.

Red cell membrane lipid composition was altered with limited incorporation of n-3 fatty acids and significant changes in cholesterol and tocopherols. Most striking was an increase in membrane α- and γ-tocopherols during the FOC period when they received FOC but no increase in vitamin E (TABLE 2). Cellular α-tocopherol was reduced during the FOC period, probably reflecting utilization, and then again elevated with the daily 200 IU vitamin E capsule. Apparently a metabolic control mechanism specifically modulated membrane tocopherol content, thereby homeostatically insuring membrane integrity despite the high PUFA content. Chautan *et al.*[15] recently reported a similar effect in rat heart membranes but not liver membranes. These results may also indicate membrane homeostasis involving α-tocopherol.

TABLE 2. Plasma and Erythrocyte, Cellular and Membrane, Vitamin E Contents (means ± SEM)

	Placebo	Fish Oil	Fish Oil + Vitamin E
	plasma: (μmol/L)		
α-tocopherol	24 ± 0.94[b]	20 ± 0.70[c]	27 ± 0.94[a]
γ-tocopherol	1.91 ± 0.12[b]	3.59 ± 0.29[a]	2.00 ± 0.18[b]
	cell: (nmol/mL packed cells)		
α-tocopherol	4.89 ± 0.15[b]	2.74 ± 0.08[c]	8.09 ± 0.40[a]
	membrane: (nmole/g protein)		
α-tocopherol	185 ± 33[c]	948 ± 169[b]	1948 ± 176[a]
γ-tocopherol	128 ± 28[b]	405 ± 95[a]	449 ± 76[a]

[a–c] Values in the same row with different superscripts are significantly different ($p < 0.05$).

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